REMARKS

The Office Action mailed June 15, 2004, has been carefully reviewed. The amendments made as directed above are in response thereto.

Claims 24, 25, 40, 42 are currently amended. Claims 24-55 are now pending.

Claims 42-55 stand rejected under 35 U.S.C § 112 as allegedly indefinite.

Claims 24-33, 36-38, 40, 42, 47-52 stand rejected under 35 U.S.C § 102(b) as allegedly anticipated by DE 4021082.

Claims 24, 26-33, 36-37, 42, and 44-55 stand rejected under 35 U.S.C § 102(b) as allegedly anticipated by EP 0 158 441.

Claims 24-55 stand rejected under 35 U.S.C § 103(a) as allegedly obvious over DE 4021082.

Claims 39 and 42-55 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over DE 4021082 in view of EP 0158 444.

The claims as amended herein are fully supported by the application as originally filed. No new matter has been added. Reexamination, reconsideration, and allowance of the present application are respectfully requested in view of the foregoing amendments and the following additional remarks.

Rejections Under 35 U.S.C. § 112

Claims 42-55 stand rejected as indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Specifically, the Examiner pointed out that claim 42 recites several active ingredients along with "nose drops" as Markush member.

In response, Applicants have amended claim 42 to recite "rhinologics" instead of "nose drops." The priority application in its native form read "Rhinologika" which should translate to "rhinologics" instead of "nose drops." It is believed that this amendment has cured the translational error and has obviated this ground for rejection. Applicants respectfully ask that the rejection be withdrawn.

Rejections Under 35 U.S.C. § 102

Claims 24-33, 36-38, 40, 42, 47-52 stand rejected under 35 U.S.C § 102(b) as allegedly anticipated by DE 4021082. The Examiner asserts that DE 4021082 discloses skin treatment compositions containing liposomal gel. The gel allegedly contains a phospholipid, phosphatidylcholine (10%), an alcohol (0.1-20%), inositol (0.1 to 10%) and the rest water. Applicants disagree and hereby traverse.

Applicants disagree with the Examiner's characterization of DE 4021082. Applicants understand that the Examiner may not have had benefit of English language translation of DE 4021082. As requested by the Examiner, the said English language translation is hereby submitted.

DE 40210982 teaches and claims skin treatment agents containing a bilayer source, salts of organic acids, alcohol, a stabiliser and lipids. (See claim 1, page 20). DE 40210982 describes bilayer source as liposome base materials, especially phosphatidyl choline. (See page 5, paragraph 3). DE 40210982 further defines lipids as consisting of at least one native oil, (partially) synthetic oil, carboxylic acid esters, liquid wax esters, and oily hydrocarbons. (See page 6, last paragraph). DE 40210982 further defines "salts of organic acids" as alkali salts of carboxylic acids – especially weak physiological carboxylic acids such as palmitic acid, stearic

acid or mixtures thereof. DE 40210982 further teaches that the "salts of organic acids" may also consist of acylated hydrolysates of collagen, elastin, casein, keratin or hydroxyproline. (See page 7, paragraph 3 and page 8, paragraph 4). DE 40210982 further defines the alcohol component of it skin treatment agent as ethanol, and other straight chained or branched-chain alcohols or polyalcohols such as propanol, isopropanol, 1,2,-propylene glycol, 1,3,-butylene glycol or glycerine. (See page 8, paragraph 6). DE 40210982 further defines the stabilizer component of its skin treatment agent as consisting of urea, monosaccharides, other saccharides or mixtures thereof. (See page 9, paragraph 2).

In terms of relative composition of its skin treatment agent, DE 40210982 teaches that its bilayer source may range anywhere from 01.0 – 10% by weight. (See page 10, last paragraph). Anticipation under Section 102 can be found only if a reference shows exactly what is claimed. *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed.Cir. 1985). Applicants assert that since the present invention does not teach a formulation containing a salt of organic acids, lipids and stabilizer within the meaning of those terms in DE 40210982, anticipation under 35 U.S.C § 102 does not apply. In particular, for at least the fact that the phospholipid composition of the phospholipid gel of the present invention is greater than 10% to about 60%, as amended, this ground for rejection does not apply. Applicants respectfully ask that the rejection be withdrawn.

Also, claims 24, 26-33, 36-37, 42, and 44-55 stand rejected under 35 U.S.C § 102(b) as allegedly anticipated by EP 0 158 441. The Examiner asserts that EP 0 158 441 discloses a composition containing 45% lecithin, 36% ethylene glycol or propylene glycol and 0.9% glucose. The Examiner further asserts that EP 0 158 441 teaches the use of phosphate buffer of pH 7.4,

prepared in N_2 atmosphere, and that the drugs [sic] taught are insulin. Applicants differ strongly with the Examiner's characterization of the teachings of EP 0 158 441 and respectfully traverse this ground for rejection.

As disclosed and claimed, EP 0 158 441 teaches a pro-liposomal formulation which spontaneously forms vesicles or liposomes in the presence of **excess water** comprising at least one membrane lipid, at least one water-miscible organic liquid which is a solvent for the lipid, and up to 40% by weight of water. In particular, EP 0 158 441 provides a pro-liposome composition and a method of converting that to an **aqueous liposome dispersion** by addition of aqueous fluid with agitation. (See page 4, lines 11-14). The liposomal dispersion of EP 0 158 441 is stated to be of use as carriers of compounds having biological property. (See page 9, lines 23-25). In the disclosure of EP 0 158 441, glucose was used to model the drug entrapping properties of the liposomal dispersion. Insulin was also mentioned as an example of a biologically active compound capable of being entrapped by the liposomal dispersion of EP 0 158 441. It is therefore more apropos to state that EP 0 158 441 teaches a pro-liposomal composition capable of, and demonstrably entrapping glucose than to assert, with all due respect, that the pro-liposomal composition of EP 0 158 441 contains glucose or insulin, within the meaning of the present invention. The glucose which the Examiner asserts to be taught by EP 0 158 441 is extrinsic, as in not being an integral part of the pro-liposomal composition of EP 0 158 441. In particular, it is useful to think in terms of how much glucose is trapped within the liposomal vesicles and how much glucose exist in the extra-liposomal space.

In contrast, the present invention discloses a phospholipid gel, which is stabilized against liquefaction by adding a tetrahydric, pentahydric or hexahydric alcohol or sugar. In that sense, the tetrahydric, pentahydric or hexahydric alcohol or sugar alcohol is an integral component of

the phospholipid gel of the present invention used to stabilize the phospholipid gel of the present invention against liquefaction. In contrast, the pro-liposomal composition of EP 0 158 441 is designed to be used in a liquefied media.

Moreover, EP 0 158 441 teaches the use of "water miscible liquid which is a solvent for its membrane lipid," preferably an aliphatic alcohol such as glycerol, propylene glycol, ethanol, isopropyl alcohol, methanol, butanol, ethylene glycol. (See page 6, lines 10 – 15). There is no teaching or suggestion anywhere in EP 0 158 441 that the "water miscible liquid which is a solvent for its membrane lipid" must contain at least one dihydric or trihydric C_2- C_4 alcohol and at least one polyhydric alcohol. Applicants fail to find support for the Examiner's assertion that the glucose allegedly "contained" in EP 0 158 441 should be construed other than liposome-entrapped glucose as taught by EP 0 158 441.

For at least the fact that the pro-liposomal formulation of EP 0 158 441 does not contain glucose as taught by the present invention, and as construed by the Examiner, Applicants assert that the rejection under 35 U.S.C. § 102(b) is in error and respectfully ask that it be withdrawn.

Rejections Under 35 U.S.C. § 103(a)

Claims 24-55 stand rejected under 35 USC 103(a) as being unpatentable over DE 4021082. The Examiner asserts that DE 4021082 discloses skin treatment compositions containing liposomal gels and that the gels contains a phosphotidylcholine (10%), alcohol ().1 – 20%), inositol (0.1-10%) and the rest water. As explained above, the Examiner's characterization of DE 40210982 is in error probably due to not having the benefit of the English translation of that patent.

DE 40210982 teaches and claims skin treatment agents containing a bilayer source, salts of organic acids, alcohol, a stabilizer and lipids. The present invention does not teach the use of salts of organic acids, nor of lipids, nor a stabilizer within the asserted meaning of those terms in

DE 40210982. In particular, there is no teaching or suggestion, nor is it within the skill of an artisan that withholding salts of organic acids and lipids on the basis of the teachings or suggestions of DE 40210982 would lead to the phospholipid gels of the present invention having its unexpected results.

Morever, DE 40210982 teaches that stabilization of phosphotidylcholine compositions against auto-oxidation is problematic and that while ordinary anti-oxidants such as vitamins C and E may stabilize compositions having 0.1 to 2% by weight of phosphatidylcholine, stability against auto oxidation is difficult to achieve at contents of 2-10 wt % phoshpatidylcholine. (See page 4, paragraph 4). As stabilizers against auto-oxidation, DE 40210982 teaches the use of urea and or monosaccharides such as inositol. (See page 9, paragraph 2). If anything, DE 40210982 teaches away from the use of phospholipids comprising greater than 10 wt % of the formulation because of the danger of auto-oxidation.

There is no teaching or suggestion that on the basis of DE 40210982 , one could raise the phospholipid compositions to greater than 10 % to about 60%, and additionally withhold the use of lipids and salts of organic acids which were taught by DE 40210982 as necessary ingredients, and arrive at the present invention.

Further nowhere was it taught or suggested that the phospholipid formulation having greater than 10% to about 60% phospholipid can be stabilized against liquefaction by the use of tetrahydric, pentahydric, hexahydric and sugar alcohols.

In particular, known phospholipid gels have the disadvantage that they can liquefy on incorporation of a pharmaceutical, buffer or salt, in particular, if readily soluble substances such as diphenhydramine HCl are incorporated. In these cases, the preparations may flow even under their own weight. Therefore, an object of the instant invention was to provide a phospholipid gel having a high stability on application to the skin and in the presence of an incorporated pharmaceutical, buffer or salt.

Accordingly, Applicants found that this problem can be solved by incorporating into the phospholipid gel a tetra-, penta- or hexahydric alcohol and or sugar, thus stabilizing the gel against liquefaction as demonstrated in examples 3-5 of the instant application.

For at least the fact that DE 40210982 did not teach nor suggest that the stability of phospholipid gels against liquefaction could be increased by incorporation of at least one tetra-,

penta- or hexahydric alcohol and/or at least one sugar, Applicants hold that claims 24 – 55 are patentable over DE 40210982 . Applicants respectfully request the withdrawal of this ground for rejection.

Also, claims 39 and 42-55 stand rejected under 35 U.S.C. § 103(a) as unpatentable over DE 4021082 in view of EP 0158444. According to the Examiner, what is lacking in the teachings of DE 40210982 is the use of buffer and the use of inert atmosphere to prepare phospholipid formulations. The Examiner asserts that the deficiency in DE 40210982 is cured by EP 0158444.

In the first place, DE 40210982 and EP 0158444 are not even properly combinable. Whereas DE 40210982 teaches skin treatment compositions comprising phospholipids stabilized against auto-oxidation, EP 0158444 teaches pro-liposomal formulations comprising phospholipids capable of forming liposomes when **agitated in excess water** and for use as drug carrier. Thus, while DE 40210982 is concerned with cosmetic applications in topical media, EP 015844 is concerned with drug delivery applications in biological fluids. Applicants assert that there would be no motivation or suggestion to apply the use of buffer and inert atmosphere of EP 0158444 in DE 40210982 to attempt to arrive at the instant invention. Moreover, the asserted combination would still not arrive at the present invention.

Since claims 39 and 42-55 depend directly or indirectly from claim 24, and since as shown above, claim 24 is patentable over DE 4021082 either alone or in combination with EP 0158444, it is asserted that this ground for rejection is now moot. Applicants respectfully ask that this rejection be withdrawn.

CONCLUSION

In view of the foregoing Applicants submit that there is no basis for applying the previous rejections to the pending claims and withdrawal of the rejections is respectfully requested. The claims are believed to be in condition for allowance, and Applicants earnestly solicit from the Examiner early notification of allowability.

Should the Examiner have any questions or believe a personal or telephonic interview may be in order, he is invited to contact the undersigned at his earliest convenience.

Respectfully submitted,

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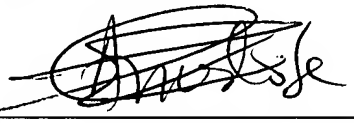
By: 

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